Increased Vitamin D Binding Protein Expression in JIA Patients Suffering Disease Extension

Proportion of women eligible for BMD and for treatment, according to the algorithms proposed for women from the UK.

	N	Prior fracture (%)	> AT and < IT (n, %)		At least 1 Risk Factor (a)	Total eligible for assessment (n; %) [>AT,<IT or at least 1 Risk Factor] (a)		> IT after DXA (n; %)		>1 Risk Factor (n; %)	Total eligible for treatment (n; %) [Prior Fracture or > T]	
			Major	Hip		Major	Hip	Major	Hip		Major	Hip
50-54 years	173	28 (16.0%)	4 (2.3%)	36 (24.5%)	24 (14.0%)	36 (24.5%)	38 (25.9%)	2 (1.2%)	14 (8.1%)	37 (21.1%)	28 (16.2%)	35 (20.2%)
55-59 years	204	45 (17.4%)	2 (0.8%)	43 (20.2%)	17 (6.6%)	43 (20.2%)	44 (20.7%)	6 (2.3%)	14 (5.5%)	52 (20.2%)	47 (23.0%)	47 (23.0%)
60-64 years	277	71 (25.6%)	6 (2.2%)	25 (12.1%)	11 (4.0%)	25 (12.1%)	26 (12.6%)	1 (0.4%)	11 (4.0%)	78 (28.2%)	71 (25.6%)	74 (26.7%)
65-69 years	206	54 (25.8%)	3 (1.5%)	9 (5.8%)	9 (4.4%)	9 (5.8%)	10 (6.5%)	5 (2.5%)	16 (7.8%)	59 (28.2%)	54 (26.2%)	59 (28.6%)
70-74 years	177	42 (23.0%)	30 (17.2%)	12 (8.5%)	57 (32.8%)	12 (8.5%)	37 (26.2%)	1 (0.6%)	7 (4.0%)	46 (25.1%)	42 (23.7%)	46 (26.0%)
75-79 years	183	71 (37.6%)	58 (32.4%)	4 (3.4%)	69 (38.5%)	4 (3.4%)	23 (19.5%)	4 (2.2%)	20 (11.2%)	78 (41.3%)	72 (39.3%)	78 (42.6%)
≥80 years	97	47 (46.1%)	37 (40.2%)	3 (5.5%)	29 (31.5%)	3 (5.5%)	13 (23.6%)	3 (3.3%)	9 (9.8%)	49 (48.0%)	47 (48.5%)	49 (50.5%)
TOTAL	1,353	358 (25.7%)	140 (10.3%)	132 (12.8%)	216 (16.0%)	132 (12.8%)	191 (18.5%)	22 (1.6%)	91 (6.7%)	399 (28.6%)	361 (27.4%)	388 (29.5%)

(a) Excludes women with a prior fracture

Background: Osteoporotic fractures and falls are as heads and tails of a coin. Among the elderly, the greatest risk of fracture comes from falls, rather than osteoporosis, hence, bone mineral density measurement should not be used alone to estimate fracture risk or guide treatment decisions. Evidence shows that at least 15% of falls in older people can be prevented, with individual trials reporting relative reductions of up to 50%. We developed a model that predicts the falls risk among patients referred for bone mineral density using variables that are easily assessed in clinical practice.
Methods: As part of the integrated osteoporosis and falls service, patients admitted to the hospital with low trauma fracture had their bone mineral density assessed. In addition to DXA scanning, fracture risk assessment using FRAX (before and after the occurrence of the fracture), as well as falls risk factors were analyzed. The independent predictive value of the different risk factors for the occurrence of falls was assessed using logistic regression analysis. A prediction scoring system was developed using data from a cohort of 106 patients. 102 osteoporotic patients without history of falls or fracture were also assessed as control group. The diagnostic performance of the prediction model was evaluated using the area under the curve (AUC). The developed prediction model was internally validated.
Results: Falls risk was significantly higher among the osteoporotic patients who sustained fractures in comparison to the control group ($P < 0.01$). The risk factors significantly correlated with an increased risk of falls were: history of > 1 fall in the last 12 months (regression coefficient 2.2), slowing of the walking speed/ change of the gait (1.6), impaired vision (1.2), weak grip strength (1.1), loss of balance (1.2). Cut off point of 3.5 achieved the best sensitivity and specificity (0.918 and 0.86 respectively, PPV85.9) and was indicative of high falls risk. A score of 2.0-3.5 was indicative of moderate risk.
Conclusions: The findings indicate that evaluation of falls risk based on risk factor profiles of individual patients can help physicians identify high risk osteoporotic patients and assist with decisions concerning falls prevention and patient management. Also, these results emphasize the importance of performing a falls risk assessment for all osteoporotic patients, in parallel with bone mineral density measurement, on regular basis as part of their assessment and management.
Disclosure statement: All authors have declared no conflicts of interest.

142. BENEFIT OF USING FRAX TO TARGET DXA USE IN A SPANISH POPULATION

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Background: Assessment (AT) and intervention thresholds (IT) and management algorithms have been proposed for the UK based on fracture probability from FRAX. A version of it is available for the Spanish population, which we applied, using the UK AT, IT and algorithms, in a sample from Barcelona (Spain) to assess the effect of FRAX in reducing the number of DXA requested.
Methods: The FRIDEX database at the Vall d'Hebron Hospital (Barcelona) includes all patients who underwent DXA scanning from 1999. At the time of scanning, questionnaires were administered: age, fractures, smoking, alcohol, family history of hip fracture (HF), rheumatoid arthritis, other secondary causes of osteoporosis and steroid exposure was collected. Height and weight were measured.All patients then underwent DXA measurement using a Lunar GE ''Prodigy Advance''. We used the NOGG UK FRAX to classify patients into low, intermediate and high risk before and after DXA.
Results: 1,353 postmenopausal women, ≥50 years,consecutively attended the DXA department (June/2008-May/2009), referred by their GP or an specialist. Mean age: 65.47 yrs ± 9.31, weight: 67.80 ± 37.32 kg and height: 156.12 ± 39.73cms. 159 (11.8%) women had Osteoporosis (OP) at Femoral Neck, and 853 (65.8%) had Osteopenia (T < −1.5).

358 (25.7%) had a prior fracture at baseline. 56 (4.0%) had a family antecedent of HF, 104 (7.5%) were smokers and none drank ≥3 alcohol units per day. 23 (1.7%) suffered from Rheumatoid Arthritis and 7 (0.5%) from any other condition considered as cause of Secondary OP in FRAX. 61 women (4.5%) had been exposed to oral corticoids and 458 (32.9%) to anti-resortive drugs.

The median HF probability before DXA was 0.9 ± 2.9 and 0.7 ± 3.0 afterwards. Other major fracture probability was 4.3 ± 5.3 and 4.0 ± 5.1 after DXA.

Using hip risk probability AT, 18 women changed from low to high risk after DXA and 23 changed from high to low risk. According to other major fractures risk probabilities, only 2 (0.2%) women changed from low to high risk and only 4 were considered as high risk before DXA; from these, 2 changed from high risk pre-DXA to low risk.
Conclusions: The use of FRAX would have saved 992 DXA scans and is a useful clinical tool to predict osteoporosis in the Spanish population.
Disclosure statement: All authors have declared no conflicts of interest.

Paediatric and Adolescent Rheumatology

143. KNEE JOINT IN JIA: A PROSPECTIVE EVALUATION OF CLINICAL EXAMINATION, ULTRASOUND AND MRI ASSESSMENT. A NEWLY DEVELOPED KNEE MRI SCORING SYSTEM IN JIA

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Background: We prospectively compared agreement between clinical, ultrasound (US) and MRI assessments of the knee joints in children with juvenile idiopathic arthritis (JIA).
Methods: Three hundred and thirty one knees from 48 children over a period of 2 years, affected by JIA with knee arthritis, were assessed clinically and ultrasonographically on the same day, using a semi-quantitative scoring system from 0 to 3 (0: normal; 1: mild; 2: moderate; 3: marked) for swelling and effusion, respectively. A subgroup of these children (25) with a total of 40 knees had matching MRI scans obtained within 0 to 14 days from clinical and US examinations. For those, US and MRI scans (T1 weighted images) were scored 0-3 for effusion, synovial hypertrophy, bone oedema and bone erosions, using for the first time our newly developed knee MRI scoring system.
Results: A moderate agreement for effusion was found between the 331 knees assessed clinically and ultrasonographically (linear weighted Kappa: 0.54). Out of the 260 clinical normal knees, 30 (11.5%) had mild to moderate effusion on US and 89 (34.2%) had trace

of effusion. In the subgroup of 40 knees that had matching US and MRI scans it was demonstrated a good agreement for effusion (linear weighted Kappa: 0.66) and a moderate agreement for synovial hypertrophy (linear weighted Kappa: 0.47). The inter-observer US agreement was very good for effusion (linear weighted kappa: 0.87) and good for synovial hypertrophy (linear weighted kappa: 0.68). The intra-observer MRI agreement was good for effusion (linear weighted kappa: 0.73) and very good for synovial hypertrophy (linear weighted kappa: 0.85).

Conclusions: A significant number of knee joint effusions are missed on clinical examination. Musculoskeletal US is a simple, cheap, non invasive, rapid and effective method of detecting joint synovitis in JIA and should be used: as an adjunct to clinical examination especially when joint injections are being considered and to avoid under-diagnosis; when clinical examination is negative and symptoms are equivocal for active arthritis; to identify the site for the intra-articular injection; at follow-up to assess treatment's efficacy. In our experience it is also very well tolerated by children. Normal data on Paediatric knees are needed to demonstrate whether a small amount of synovial fluid is present.

Comparison between clinical and US scores (0-3) for swelling and effusion respectively

US EFFUSION SCORE	CLINICAL	SWELLING	SCORE	
	0	1	2	3
0	230	5	0	0
1	25	27	7	0
2	5	2	12	8
3	0	0	3	7

Disclosure statement: All authors have declared no conflicts of interest.

144. INCREASED VITAMIN D BINDING PROTEIN EXPRESSION IN JIA PATIENTS SUFFERING DISEASE EXTENSION

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Background: Juvenile idiopathic arthritis (JIA) comprises a poorly understood group of chronic, childhood onset, autoimmune diseases with variable clinical presentations, outcomes and therapeutic responses. Current laboratory tests are unable to flag those patients at a higher risk of disease spread to multiple joints, who could benefit form earlier therapy to prevent joint damage. This study was focused on profiling the synovial fluid (SF) proteome associated with disease extension from oligo- to polyarticular status by a difference gel electrophoresis (DIGE) approach.

Methods: To construct a discriminant model, SF samples from 55 JIA patients were analysed: 30 oligo-, 8 extended oligo- and 17 polyarticular disease. Initial SF samples from each patient were labeled with Cy dyes and subjected to protein separation by 2-DE. The ability to distinguish patients at risk of disease extension by a select group of proteins was illustrated by multivariate analysis methods. Proteins over expressed with a two-fold difference between patient subgroups were identified by MALDI-TOF. Specific antibodies were used to validate putative biomarker expression in synovial fluid by western immunoblotting and in synovial membrane (SM) by immunohistochemistry.

Results: Samespots software analysis of SF gel scans was used to highlight joint-specific proteins which were differentially expressed across disease classifications. Hierarchical clustering based on the expression levels of a previously selected set of 40 proteins matched across the three clinical subgroups segregates the extended oligoarticular patients. Proteolytic fragments of apolipoprotein AII, complement component C3c and vitamin D binding protein were identified ($P < 0.05$) amongst the discriminatory proteins. Apolipoprotein AII and vitamin D binding protein were expressed at significantly higher levels in the polyarticular patients, $P = 0.046$ and $P = 0.019$ respectively, both with a perivascular distribution in the SM.

Conclusions: Synovial fluid proteome profiles have been used to flag JIA patients at risk of disease spread. The panel of identified proteins may play a role in spread of joint inflammation. With further validation, these putative prognostic biomarkers could improve the clinical management of patients

Disclosure statement: All authors have declared no conflicts of interest.

145. A PROSPECTIVE EVALUATION OF CLINICAL AND ULTRASOUND FINDINGS IN ANKLE DISEASE IN JUVENILE IDIOPATHIC ARTHRITIS

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Background: Intra-articular corticosteroid (IAC) injections are frequently used by clinicians in the management of joint disease in JIA with good effect. However, remarkably little has been written about the effectiveness of IAC injection in ankle disease in JIA. Our experience and of others, is that the response for ankle disease is disappointing. The poor result from IAC injection may be due to the incorrect identification of the structures involved. We compared prospectively clinical examination of the ankle structures with ultrasound (US) findings.

Methods: In 42 children with JIA (F/M = 25/17, mean age 11.3 years, range 2.3-22.3), a total of 61 swollen/painful ankles were assessed clinically and ultrasonographically. An accurate clinical examination of the entire ankle joint, focusing especially on 3 regions - main ankle joint (tibiotalar joint), medial tendons (tibialis posterior tendon group) and lateral tendons (peroneal tendons) - has been performed. US images were obtained by longitudinal and transverse scans with knee in 45 degrees of flexion. Clinical and US findings were both scored 0-3 (0: normal; 1: mild; 2: moderate; 3: severe). Involvement of other structures such as talonavicular, tibialis anterior and subtalar involvement was recorded.

Results: US demonstrated no signs of tibiotalar joint effusion in 14 out of 43 ankles considered clinically involved. For the medial tendons, US showed tenosynovitis in 13 ankles out of 31 thought to be clinically normal; and for the lateral tendons, of the 19 deemed to be clinically involved, less than 50% had involvement on US. Very poor agreement was observed comparing the clinical and US scores for the 3 regions: tibiotalar joint - kappa 0.3; medial tendons - kappa 0.24; lateral tendons - kappa 0.25. With regards to other ankle structures, only 39% of the subtalar joint considered clinically involved were deemed abnormal on US. Finally, of the 10 ankles with talonavicular ultrasonographical effusion, only 2 were considered to be clinically involved. Of interest, from the US scans, in only 12 ankles (19.7%) the tibiotalar joint was involved alone, whereas in 37 ankles (60.7%) both the tibiotalar and tendons were involved. Conversely, in 10 ankles (16.4%) tendons alone were involved.

Conclusions: This is the first prospective assessment of ankle disease in JIA. Clinical examination of the ankle region in children with JIA is inadequate in identifying the structures involved. US assessment on that area prior to any therapeutically intervention should be considered to improve the outcome.

Table. Agreement between involved *vs* non-involved according to the clinical and US findings.

	Clinical normal / US normal	Clinically normal / US abnormal	Clinically abnormal / US normal	Clinically abnormal / US abnormal
Tibiotalar joint	18 / 10	18 / 8	43 / 14	43 / 29
Tibialis post tendon group	31 / 18	31 / 13	30 / 11	30 / 19
Peroneal Tendons	42 / 33	42 / 9	19 / 11	19 / 8

Disclosure statement: All authors have declared no conflicts of interest.

146. ASSOCIATION OF ERAP1 WITH ENTHESITIS RELATED ARTHRITIS

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Background: The endoplasmic reticulum aminopeptidase 1 (ERAP1) gene, formerly known as ARTS1, shows robust association with ankylosing spondylitis (AS). HLA-B27 plays a central role in the pathogenesis of many spondyloarthropathies and in particular AS. The enthesitis related arthritis (ERA) subtype of juvenile idiopathic arthritis (JIA) is characterized the association of enthesitis and arthritis. It may go on to affect the sacroiliac and spinal joints, with symptoms similar to AS. It mainly affects male individuals and most patients are HLA-B27 positive. The aim of this study was to test whether ERAP1, the confirmed AS susceptibility locus, also predisposes to the ERA subtype of JIA.

Methods: The SNP, rs30187, a non-synonymous SNP in the ERAP1 gene was genotyped in JIA cases ($n = 1054$) and healthy controls ($n = 2390$). Genotype and allele frequencies were compared between cases with JIA and controls using the Cochrane-Armitage trend test implemented in PLINK and allelic odds ratios (ORs) and their 95% confidence intervals (CIs) calculated. Allele frequency differences between the seven ILAR subtypes were assessed using $\chi 2$ tests on the 7 x 2 tables.
Results: The SNP in the ERAP1 gene, rs30187, was not significantly associated with JIA overall (ptrend = 0.73 OR 1.03 95% CI 0.92-1.14). The SNP showed significant allele frequency differences ($P = 0.01$) between the ILAR subtypes. Reanalysis of the SNP stratifying by subtype found that the difference was driven by the association of the enthesitis related arthritis (ERA) subtype with rs30187 (ptrend = 0.003 OR 1.7 95% CI 1.19-2.44). None of the other subtypes showed evidence for association with the SNP.
Conclusions: We present subtype specific association of the ERAP1 gene and ERA, none of the other subtypes showed association with the SNP. This finding will require validation in independent JIA data sets. ERAP1 encodes a multifunctional aminopeptidase, but the mechanism by which it affects disease risk is yet to be determined. It may play a role in trimming peptides before loading into nascent HLA class I molecules, or alternatively through its function in cleaving pro-inflammatory cytokine receptors, such as TNFR1, IL1R2 and IL6R, from the cell wall.
Disclosure statement: All authors have declared no conflicts of interest.

147. USE OF BIOLOGIC AGENTS IN ADULTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Biologic agents are increasingly used in rheumatological practice although only etanercept and adalimumab have JIA as a licensed indication in children. NICE guidance exists for etanercept in polyarticular JIA but is limited to 4-17 year olds. Over one third of children with JIA will continue to have active disease into their adult years [1] and many will transfer to adult services with an ongoing need for biologics. Furthermore, patients with JIA may develop new flares of disease in their adult years requiring immunosuppression. No guidance exists for the use of biologic agents in adults with JIA. Our aim was to describe our experience of biologic use in a previously described adult JIA population [2].
Methods: This retrospective case notes audit describes the use of biologic therapy in an adult JIA clinic set up in 1996. A piloted proforma based on NICE guidance for etanercept in JIA was used to collect data on demographics, disease duration, disease modifying drugs and biologics, adverse events and changes in treatment. The study had Trust approval and was registered as an audit of clinical practice.
Results: 31/184 patients (17%) have received biologic therapies to date. Details were available for 27/31 patients; 19/27 (70%) were female with a median age of 27 years (range 18 - 49), median age of disease onset of 10.5 years (range 1 - 16) and a predominance of poly JIA (16/27 (59%)). The median disease duration prior to first biologic was 15 years (range 1 - 36); 6 patients (22%) were < 16 and 21 (78%) > 16 years when the first biologic was commenced. All paediatric cases were recorded on the BSPAR Biologics Registry and many adult patients on the BSRBR. In 25/27 cases the first agent was etanercept and in 2/27 infliximab (for active uveitis). Indications for use of etanercept included persistent active disease (> 5 joints) and failure / intolerance to methotrexate as per NICE guidance. 11/27 (41%) patients switched to a second anti-TNF (8/11 with poly JIA) with median time to switch 2.5 years (range 0.3 - 5.25). Initial switch was due to waning of response in 9/11, often after protracted remission, uveitis flare n = 1 and infusion reaction n = 1. Further switches of biologic agent were required in 6/27 (22%) patients (lack of response n = 5, uveitis flare n = 1).
Conclusions: Many adults with JIA have ongoing medical needs associated with persistently active disease requiring immunosuppression, including continued use of biologics in adulthood and de novo disease flares in adulthood. Adults with active JIA in this centre are managed according to NICE guidance for poly JIA in children. Guidance for the adult age group is clearly required. A waning of initially good response was noted in this group, necessitating switching to alternative agents. This highlights the need for long-term efficacy and safety studies in JIA, extending from childhood into adulthood. A survey of clinical practice in other UK units with adult JIA clinics is planned.
Disclosure statement: All authors have declared no conflicts of interest.
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148. WORKFORCE PLANNING IN PAEDIATRIC RHEUMATOLOGY IN THE UNITED KINGDOM (UK)

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Background: The British Society for Paediatric and Adolescent Rheumatology (BSPAR) recommends that all children with rheumatic disease are managed by specialist multidisciplinary teams with appropriate training in paediatric rheumatology (PRh) [1]. In the UK and many other parts of the world, adult rheumatologists have historically provided clinical care for children with rheumatic disease and increasingly there has been development of multidisciplinary PRh services working in clinical networks with adult rheumatologists or paediatricians. Recent changes in clinical training in the UK have resulted in PRh becoming a paediatric sub-speciality. Adult rheumatology trainees are no longer being trained in PRh and will be ill-equipped to manage children when incumbent adult rheumatology specialists retire.
Methods: In 2007 a questionnaire was sent to all UK adult rheumatology specialists. One aim was to identify the number of adult rheumatologists seeing children under 16 years, describe the clinical setting for consultations and to estimate numbers due to retire based on a retirement age of 65 years. This information will be used to determine future numbers of PRh consultants.
Results: The questionnaire was sent to 584 adult rheumatology specialists with 403 (69%) responding to questions about PRh service provision. 75/403 (19%) reported seeing patients aged under 16. The median (IQR) number of patients seen per month was 10 (6, 15), accounting for 931 paediatric patients seen in a year. Many rheumatologists will retire in the next 5 and 10 years (13/73 (18%) and 35/73 (48%) respectively). The majority (58/75, 78%) of respondents hold separate clinics for all paediatric patients, often alongside another health care professional (38/58 [57%] consultant paediatrician, 5/58 [9%] PRh specialist, 5/58 [9%] with both present and 7/58 [12%] with another healthcare professional). 3/58 (5%) of adult rheumatologists ran paediatric clinics without another healthcare professional present and 4/75 (5%) of all specialists seeing children did so on their own without paediatric input.
Conclusions: Throughout the UK many adult rheumatologists are involved in managing children with rheumatic disease and many within a shared care model with paediatric rheumatologists or paediatricians. Over the next 10 years a large number of adult rheumatologists who manage children with rheumatic disease will retire. Their departure will result in a large shortfall in service provision. Unless addressed urgently in workforce planning and training within PRh in the UK, along with appropriate expansion of clinical services, these changes will results in marked inequity of access to specialist care for children with rheumatic disease.
Disclosure statement: All authors have declared no conflicts of interest.
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149. INVESTIGATION OF TYPE 1 DIABETES AND CELIAC DISEASE SUSCEPTIBILITY LOCI FOR ASSOCIATION WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Autoimmune diseases affect about 1% of the population and are caused by a combination of both genetic and environmental

factors. It is now becoming clear that, despite the apparent clinical and phenotypic differences of the autoimmune diseases, they share a number of genetic risk factors. Of note there has been overlap between type 1 diabetes (T1D) and celiac disease (CD). Many of these loci are also susceptibility loci for rheumatoid arthritis (RA). There is already strong evidence suggesting that JIA shares many susceptibility loci with other autoimmune diseases, such as rheumatoid arthritis (RA), type 1 diabetes and multiple sclerosis (MS). Therefore the aim of this study was to test SNPs robustly associated with T1D or CD in a large cohort of JIA cases and controls to investigate the overlap between these diseases.
Methods: Sixteen SNPs that showed robust association ($P < 5$ x 10-7) with T1D and CD and had not been investigated previously in JIA were genotyped in JIA cases ($n = 1054$) and healthy controls ($n = 3129$). Genotype and allele frequencies were compared between cases with JIA and controls using the Cochrane-Armitage trend test implemented in PLINK and allelic odds ratios (ORs) and their 95% confidence intervals (CIs) calculated.
Results: One SNP in the Lim domain containing preferred translocation partner in lipoma (LPP) gene showed significant association with JIA (ptrend = 0.002 OR 1.18 95% CI 1.06-1.30). A second SNP, rs653178, in ATXN2 showed a trend towards association with JIA however this was not significant after correction for multiple testing (ptrend = 0.02 OR 1.13 95% CI 1.02-1.25). SNPs in this region, have previously shown evidence for association with JIA in a US cohort. A SNP, rs17810546, in IL12A showed a significant allele frequency difference ($P = 0.03$) between the subtypes and this was driven by a strong association with enthesitis related arthritis (ERA) subtype (ptrend = 0.005 OR 1.88 95% CI 1.2-2.94).
Conclusions: We present evidence for a novel JIA susceptibility locus, LPP. LPP has a number of known functions including cell migration and adhesion, has transcriptional activation capacity and has recently been identified as a substrate of protein-tyrosine phosphatase 1B. We present confirmatory evidence for association of the SH2B3/ATXN2/c12orf30 region with JIA. In addition we identify a subtype specific association of IL12A with ERA. All findings will require validation in independent JIA data sets.
Acknowledgements: Childhood arthritis prospective study (CAPS), UKRAG consortium and BSPAR study group.
Disclosure statement: All authors have declared no conflicts of interest.

150. ASSOCIATION OF THE CCR5 GENE WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: CC chemokine receptor 5 (CCR5) has been shown to be important in the recruitment of T helper cells to the synovium, where they accumulate and drive the inflammatory process and the consequent synovitis and joint destruction. A 32 base-pair insertion/deletion variant (CCR5delta32) within the gene leads to a frame shift and a non-functional receptor. CCR5delta32 has been investigated for association with juvenile idiopathic arthritis (JIA) with conflicting results. The aim of this study was to investigate whether CCR5delta32 is associated with JIA in a UK population and to combine our data with previously published studies in a meta-analysis.
Methods: The CCR5delta32 variant was genotyped in JIA cases ($n = 1054$) and healthy controls ($n = 2390$). Genotype and allele frequencies were compared between cases with JIA and controls using the Cochrane-Armitage trend test implemented in PLINK and allelic odds ratios (ORs) and their 95% confidence intervals (CIs) calculated. The Cochran-Mantel-Haenszel test was used to perform a meta-analysis of the three cohorts and a test for heterogeneity between cohorts was carried out using the Breslow-Day test.
Results: CCR5delta32 was significantly associated with protection from developing JIA, ptrend = 0.006, OR 0.79 95% CI 0.66-0.94. The meta-analysis of all published case-control association studies confirms the protective association with JIA ($P = 0.001$ OR 0.82 95% CI 0.73-0.93).
Conclusions: We present evidence for a protective association of the CCR5delta32 in a UK JIA case control cohort which is strengthened by combining data from two previous studies by meta-analysis. Further investigation into how this gene contributes to JIA pathogenesis is now required. The CCR5delta32 is a functional variant determining the number of receptors on the surface of T cells and its hypothesized that the level of CCR5 expression could influence the migration of pro-inflammatory T cells into the synovium and thus lead to susceptibility to JIA.
Acknowledgements: Childhood arthritis prospective study (CAPS), UKRAG consortium and BSPAR study group.
Disclosure statement: All authors have declared no conflicts of interest.

Rheumatoid Arthritis: Treatment

151. SHOULD WE BE LOOKING MORE CAREFULLY FOR METHOTREXATE INDUCED LIVER DISEASE?

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Background: UK guidelines and a 'Rheumatology' editorial suggest that liver function tests (LFTs) alone remain a satisfactory method for methotrexate (MTX) monitoring in rheumatoid arthritis (RA). Recent literature also suggests no difference in hepatotoxity between MTX treated RA and psoriatic arthritis (PsA) patients. We describe 3 cases of liver fibrosis / cirrhosis missed by conventional monitoring.
Methods: Case 1: 71 yr old female, RA 35 yrs. Presented 2005. Previous breast cancer. Alcohol < 1 unit/week. Rx MTX for 20 years, up to 25mg weekly. Leflunomide (Lef) 10 mg od added 3 mths previously. LFTs normal, P3NP 6.6. 2005-6 RA well controlled, normal LFTs. Repeat P3NP 2006 11.7. Liver ultrasound (US): normal echogenicity and hepatic and portal vein flow. Attempts to stop Lef were unsuccessful and led to use of rescue depomedrone. Developed diabetes. Sept 2007 LFTs normal, albumin 35. Feb 2008: admitted with ascites, ALT 41, albumin 31, bilirubin 24. CT liver normal, US suggested fatty change with normal portal flow. Biopsy showed established cirrhosis on a background of steatohepatitis. MTX and Lef stopped. June 2008: fatal pneumonia.

Case 2: 69 yr old male. RA 2007; previous type II diabetes Rx insulin. On simvastatin. Alcohol < 1 unit/week. eGFR 60. LFTs normal. Rx MTX 12.5 mg/week + folic acid. July 2008 ALT 83: MTX ↓ 10 mg, Oct 2008 ALT 89: MTX ↓7.5 mg. Nov 2008 ALT 69. Dec 2008 - Aug 2009 ALT 70, 91, 67, 65, 52 (ie < x2 normal). Aug 2009 ALT 38, alb 27. Sept 2008 ALT 85, albumin 22, INR 1.7.US: shrunken liver. Full liver screen negative. Developed spontaneous bacterial peritonitis. Died Sept 2009.
Results: Case 3: 63 yr old female, presented 1999. PsA diagnosed 1993, Rx MTX 7.5mg weekly. Alcohol < 1 unit/week. 1996 'routine' liver biopsy performed (i.e. after 3 yrs MTX), result missing. 1997 US liver normal. Jan 1999: AST 69. Previous liver biopsy retrieved: steatosis + perivascular fibrosis. MTX stopped. LFTs normalized and remain normal.
Conclusions: The risk of liver damage in some MTX treated RA and PsA patients may be higher than we think. Patients remain on MTX long term, may resume excess alcohol consumption and may develop concommitant non alcoholic fatty liver disease and steatohepatitis (NAFLD, NASH) during the course of their illness. Polypharmacy (case 1) and diabetes (cases 1 and 2) may be further risk factors. Normal LFTs and US may offer false reassurance. However, minor elevations of liver enzymes may point towards ongoing fibrosis (Case 2). P3NP is used in psoriasis but not in RA because of the confounding factors of disease activity and joint erosion. However, normal values may give some reassurance. US is unreliable as a guide to fibrosis, but more sensitive scans, including Fibroscan, offer promise. Our cases suggest that there may be at risk MTX treated RA and PsA patients who require more detailed liver monitoring.
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152. RHEUMATOID ARTHRITIS AND BRONCHIECTASIS: TREATMENT WITH RITUXIMAB

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Background: There is an increased prevalence of bronchietasis in patients with Rheumatoid Arthritis (RA). RA with concomitant